## REMARKS

The Office Action of June 17, 2003 has been reviewed and its contents carefully noted. Reconsideration of this case, as amended, is earnestly requested. Claims 1-22 and 24-26 remain in this case, claims 2-8, 10-15, 17-22 and 24-26 being amended by this response. The amendment of the claims is supported by the original claims and throughout the specification; no new matter has been added.

### Sequence Listing

The Examiner maintains that a substitute sequence listing is required, including the sequence of GenBank Accession No. T46645, and further maintains that sequence identifiers are required in claims 24-26.

Enclosed herewith Applicant submits its substitute Sequence Listing in both paper and computer-readable form, as helpfully suggested by the Examiner. Claims 24-26 are hereby amended to include sequence identifiers, as helpfully suggested by the Examiner.

It is noted that the sequence of GenBank Accession No. T46645 in the Sequence Listing was last updated at GenBank on August 4, 1998, which is before Applicant's filing date of November 16, 1999. Therefore, the sequence listing does not include any new matter. Also submitted herewith is Applicant's Statement under 37 CFR §§ 1.821 (f)-(g).

Reconsideration and withdrawal of the objection are respectfully requested.

### Objections to the Claims

Claims 2-8, 10-15 and 17-22 were objected to for various informalities. Claims 2-8, 10-15 and 17-22 are hereby amended to correct the informalities, as helpfully suggested by the Examiner. It is respectfully submitted that the objections to the claims are thus overcome. Reconsideration and withdrawal of the objections are respectfully requested.

**Rejections under 35 U.S.C. §112**

Claims 1-22 and 24-26 were rejected under 35 U.S.C. § 112, first paragraph, as lacking enablement. Applicant respectfully disagrees with the rejection, and believes that the claims, as amended, are enabled by the specification.

The test for enablement is whether the disclosure, when originally filed, contained sufficient information regarding the subject matter of the claims as to enable those of ordinary skill in the pertinent art to make and use the invention. The standard is whether the experimentation necessary to practice the invention is undue or unreasonable. In re Wands, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988). See also U.S. v. Teletronics, Inc., 857 F.2d 778, 785, 8 USPQ2d 1217, 1223 (Fed. Cir. 1988) ("The test of enablement is whether one reasonably skilled in the art could make or use the invention from the disclosures in the patent coupled with information known in the art without undue experimentation.") (emphasis added).

It is further noted that satisfaction of the enablement requirement is not precluded by the necessity of some experimentation, such as routine experimentation. The key word here is "undue" not "experimentation". In re Angstadt, 190 USPQ 214 (CCPA 1976). The fact that experimentation may be complex does not necessarily make it undue, if the art typically engages in such experimentation. In re Certain Limited-Charge Cell Culture Microcarriers, 221 USPQ 1165, 1174 (Int'l Trade Comm'n 1983), aff'd. sub nom., Massachusetts Institute of Technology v. A.B. Fortia, 774 F.2d 1104, 227 USPQ 428 (Fed. Cir. 1985). See also In re Wands, 858 F.2d at 737, 8 USPQ2d at 1404. Indeed, a considerable amount of experimentation is permissible if it is merely routine, or if the specification provides a reasonable amount of guidance to the direction in which the experimentation should proceed. In re Jackson, 217 USPQ 804 (Bd. App. 1982). Thus, the test of enablement is not whether any experimentation is necessary, but whether, if experimentation is necessary, it is undue. In re Angstadt, 537 F.2d 498, 504, 190 USPQ 214, 219 (CCPA 1976).

Further, the specification need not explicitly teach those in the art to make and use the invention; the requirement is satisfied if, given what they already know, the specification teaches those in the art enough that they can make and use the invention without "undue experimentation." Genentech, Inc. v. Novo Nordisk, A/S, 108 F.3d 1361, 1365, 42 USPQ2d

1001, 1004 (Fed. Cir. 1997); In re Vaeck, 947 F.2d 488, 495, 20 USPQ2d 1438, 1444 (Fed. Cir. 1991). Indeed, a patent need not teach, and preferably omits, what is well known in the art. In re Buchner, 929 F.2d 660, 661, 18 USPQ2d 1331, 1332 (Fed. Cir. 1991); Hybritech, Inc. v. Monoclonal Antibodies , Inc., 802 F.2d 1367, 1384, 231 USPQ 81, 94 (Fed. Cir. 1986), cert. denied, 480 U.S. 947 (1987); Lindemann Maschinenfabrik GMBH v. American Hoist & Derrick Co., 730 F.2d 1452, 1463, 221 USPQ 481, 489 (Fed. Cir. 1984).

The Examiner maintains that the claims are broadly drawn to a method of increasing the endogenous level of vitamin C in a plant by expression of a nucleic acid that encodes an enzyme in a plant biosynthetic pathway for vitamin C biosynthesis, and plants thereby obtained. The Examiner rejects the claims on the grounds that the specification does not provide guidance for the sequence of the full-length gene encoding GMPase, for wild-type plants transformed with the GMPase gene, or for methods of making stress resistant plants by transformation with a nucleic acid encoding the GMPase gene. On this basis, the Examiner maintains that undue experimentation would be required for one of ordinary skill in the art to practice Applicant's invention. Applicant respectfully traverses the Examiner's assertions.

**The specification provides ample guidance for the gene encoding GMPase**

It is respectfully submitted that Applicant's specification provides ample guidance for the full-length gene encoding GMPase. For example, the specification recites that *VTC1* (which encodes the GMPase) was fine-mapped to a position on chromosome 2 to one side of two molecular markers; 0.9 cM from marker m429 and 1.2 cM from marker nga168 (as shown in Figure 3A). Using microsatellite marker 178, which is >1 cM centromeric proximal to nga168, it was determined that *VTC1* is centromere distal to nga168 and m429. Specification at page 10 lines 14-18. Applicant's mapping data place *VTC1* within a 2 Mb region on Chr 2 that spans m429 to just beyond marker m336. Specification at page 10 lines 23-24. Further, Applicant cloned and sequenced the full-length cDNA encoding the *Arabidopsis* GDP-mannose pyrophosphorylase (EST ID #9908, GenBank #T46645). This cDNA was fully sequenced on both strands, and the sequence of the full-length cDNA encoding this protein defined all intron/exon borders. This gene contains 5 exons, with exon 1 and a small section of exon 2 being a 5' untranslated region. The ~40 kD protein inferred from this open reading frame has

59% amino acid identity with the mannose-1-phosphate guanyltransferase from *S. cerevisiae*. See Applicant's specification at page 11 lines 8-15. The foregoing data, taken together with the prior art, provide ample guidance for the full-length sequence, and repeatable methods for cloning and sequencing the full-length gene encoding GMPase, such that obtaining the full-length sequence would not require undue experimentation.

The Examiner states that the rejection may be overcome if Applicant deposit its full-length cDNA clone T517 with the American Type Culture Collection, under the terms of the Budapest Treaty. However, Applicant maintains that such a deposit is unnecessary and would be redundant, because the cDNA encoding the *Arabidopsis* GDP-mannose pyrophosphorylase (EST ID #9908, GenBank #T46645, www.ncbi.nlm.nih.gov/irx/cgi-bin/birx_doc?dbest_cu+6850) is already on deposit and can easily be obtained from the Arabidopsis Biological Resource DNA Stock Center (aims.cps.msu.edu/aims; Columbus, OH), as described in the specification. Thus, obtaining a clone of the full-length gene would not require any experimentation at all, let alone experimentation that is "undue." Thus, Applicant's specification provides ample guidance for the full-length sequence, and repeatable methods for cloning and sequencing the full-length gene encoding GMPase, such that one of ordinary skill in the art could practice the claimed invention without undue experimentation.

Applicant submits herewith its Declaration under 37 C.F.R. § 132, providing additional evidence in support of the foregoing arguments, showing that one of ordinary skill in the art would be able to practice the claimed invention without undue experimentation. See attached Declaration of Dr. Patricia Conklin.

**The specification provides ample guidance for plants transformed with a GMPase**

It is respectfully submitted that Applicant's specification provides ample guidance for wild-type plants transformed with the GMPase gene, and for methods of making stress resistant plants by transformation with a nucleic acid encoding the GMPase gene. Indeed, Applicant's specification provides real examples of transgenic plants that Applicant, in fact, transformed with the full-length gene encoding GMPase (Specification at page 14 lines 1-6), and which exhibited increased Vitamin C levels (Specification at page 16 Table 1).

Applicant's specification need not (and preferably does not) disclose that which is well known in the art. In re Buchner, 929 F.2d 660, 661, 18 USPQ2d 1331, 1332 (Fed. Cir. 1991); In re Myers, 410 F.2d 420, 161 USPQ 668 (CCPA 1969); Lindemann Maschinefabrik GMBH v. American Hoist and Derrick Co., 221 USPQ 481 (Fed. Cir. 1984). The Examiner admits that prior art by Bauw et al. (WO 98/50558) teaches *Arabidopsis* and tobacco plants transformed with a gene encoding L-galactono-y-lactone dehydrogenase (pages 15-20), an enzyme involved in vitamin C biosynthesis. The Examiner further admits that increased vitamin C levels (Table 5) and increased stress resistance (page 2 lines 16-21) are inherent properties of these plants. See Office Action of July 24, 2001 at section 16, page 9 line 21 to page 10 line 2.

The Examiner also admits that Trulson *et al.* (U.S. Pat. No. 6,143,562) teaches tomato, melon, squash and maize plants transformed with a gene encoding phosphomannose isomerase (claims 1-19 and columns 25-30), an enzyme in the vitamin C biosynthetic pathway. The Examiner further admits that increased vitamin C levels and increased stress resistance are inherent properties of these plants. See Office Action of July 24, 2001 at page 9, section 15, lines 15-20. Thus, the prior art teaches that plants can be transformed with a gene encoding an enzyme in the Vitamin C pathway and thereby produce transgenic plants having increased Vitamin C and stress resistance.

Therefore, based on the extensive teachings in the art, combined with the teachings in Applicant's disclosure (which provides real examples), it is clear that a wide variety of plants can be transformed with a gene encoding an enzyme in the Vitamin C biosynthetic pathway, thereby increasing the levels of Vitamin C and the stress resistance of the plants. Thus, combined with the extensive teachings of the prior art, Applicant's disclosure provides ample guidance for wild-type plants transformed with the GMPase gene, and for methods of making stress resistant plants by transformation with a nucleic acid encoding the GMPase gene, such that producing the transgenic plants would not require undue experimentation.

Indeed, by following the teachings in its specification, Applicant subsequently has identified another gene encoding another enzyme in the Vitamin C biosynthesis pathway, VTC4. See Ser. No. 09/909,600. The methods used to identify and isolate this second gene were

identical to those in the present specification. Thus, clearly, the present specification provides enablement for the claimed invention. See attached Declaration of Dr. Patricia Conklin.

It is respectfully submitted that the Examiner's assertion that the unpredictability associated with expression of genes in plants has not been overcome is mistaken, in that Applicant's gene encoding GMPase was, in fact, transformed into plants, thereby generating genetically engineered plants having increased levels of Vitamin C, relative to the progenitor plants. See Applicant's specification at page 13, line 24, through page 17, line 3. Thus, clearly, Applicant's GMPase can be expressed in plants, and clearly such plants have increased levels of Vitamin C, thus overcoming any alleged unpredictability.

Applicant submits herewith its Declaration under 37 C.F.R. § 132, providing additional evidence in support of the foregoing arguments, showing that one of ordinary skill in the art would be able to practice the claimed invention without undue experimentation. See attached Declaration of Dr. Patricia Conklin.

The Examiner asserts that claim 22 is directed to a method that produces a plant that is edible, yet the specification does not teach conversion from an inedible to an edible plant. Claim 22 is hereby amended to overcome the rejection.

In view of the foregoing amendments and remarks, Applicant respectfully submits that these amendments have fully addressed the Examiner's rejections, and that the claims are now in condition for allowance. Reconsideration and withdrawal of the rejection of claims 1-22 and 24-26 as lacking enablement are respectfully requested.

Claims 1-22 and 24-26 were rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Applicant respectfully disagrees with the rejection, and believes that the specification provides an adequate written description of the claimed subject matter, such that one of ordinary skill in the art would understand that Applicant had possession of the invention at the time of filing.

The test for compliance with the written description requirement is whether the disclosure as originally filed reasonably conveys to the artisan that the inventor had possession at that time of the later claimed subject matter, rather than the presence or absence of literal support in the specification for the claim language. Ralston Purina Co. v. Far-Mar-Co., Inc., 772 F.2d 1570, 1575, 227 USPQ 177, 179 (Fed. Cir. 1985) (quoting In re Kaslow, 707 F.2d 1366, 1375, 217 USPQ 1089, 1096 (Fed. Cir. 1983). The standard is whether the written description allows persons of ordinary skill in the art to recognize that the patent applicant invented what is claimed. In re Gosteli, 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989).

Whenever the issue arises, **the fundamental factual inquiry is whether a claim defines an invention that is clearly conveyed to those skilled in the art at the time the application was filed**. However, the subject matter of the claim need not be described literally (*i.e.*, using the same terms or *in haec verba*) in order for the disclosure to satisfy the description requirement. See In re Kaslow, 707 F.2d 1366, 1375, 217 USPQ 1089, 1096 (Fed. Cir. 1983). Further, the disclosure must be read in light of the knowledge of those skilled in the art, as evidenced by references available to the public prior to the filing date. In re Lange, 644 F.2d 856, 863, 209 USPQ 288, 294 (CCPA 1981).

The purpose of the written description requirement is to prevent an applicant from later asserting that he invented that which he did not. Compliance with the written description requirement is essentially a fact-based inquiry that will "necessarily vary depending on the nature of the invention claimed." Enzo Biochem v. Gen-Probe, Inc., 296 F.3d 1316, 1324, 63 USPQ2d 1609, 1613 (Fed. Cir. 2002). In Enzo Biochem, the Federal Circuit clarified that Eli Lilly did not hold that all functional descriptions of genetic material necessarily fail as a matter of law to meet the written description requirement; rather, the requirement may be satisfied if in the knowledge of the art the disclosed function is sufficiently correlated to a particular, known structure. See Enzo Biochem, 296 F.3d at 1324, 63 USPQ2d at 1613 (emphasis added).

More recently, the Federal Circuit has clearly stated that:

> "We held in Eli Lilly that the adequate description of claimed DNA requires a precise definition of the DNA sequence itself not merely a recitation of its function or a reference to a

> potential method for isolating it. 119 F.3d at 1566-67, 43 USPQ2d at 1406 (holding the disclosure of the cDNA sequence of the insulin gene of a rat did not adequately describe the cDNA sequence of the insulin gene of every vertebrate). More recently, in Enzo Biochem, we clarified that Eli Lilly did not hold that all functional descriptions of genetic material necessarily fail as a matter of law to meet the written description requirement; rather, the requirement may be satisfied if in the knowledge of the art the disclosed function is sufficiently correlated to a particular, known structure. See Enzo Biochem, 296 F.3d at 1324, 63 USPQ2d at 1613."

See Amgen v. Hoescht Marion Roussel, Inc., 65 USPQ2d 1385 (Fed. Cir. 2003).

It is respectfully submitted that many of the genes encoding GMPase (including that of *Arabidopsis* and other species), as well as the other enzymes in the Vitamin C pathway, are well known in the art and, as such, are not required to be disclosed in Applicant's specification. Furthermore, Applicant's Figure 1 and the specification at page 4, lines 12-16, disclose the enzymes in the Vitamin C pathway. Further, Applicant's specification provides ample guidance for the sequence of the gene encoding GMPase, as explained above. Thus, one of ordinary skill in the art would know that Applicant was in possession of the GMP-mannose pyrophosphorylase gene and recombinant plants transformed with this gene that express increased levels of Vitamin C.

Applicant submits herewith its Declaration under 37 C.F.R. § 132, providing additional evidence in support of the foregoing arguments, showing that one of ordinary skill in the art would understand that Applicant was in possession of the GMP-mannose pyrophosphorylase gene and recombinant plants transformed with this gene that express increased levels of Vitamin C. See attached Declaration of Dr. Patricia Conklin.

In view of the foregoing amendments and remarks, Applicant respectfully submits that these amendments have fully addressed the Examiner's rejections, and that the claims are now in

condition for allowance. Reconsideration and withdrawal of the rejection of claims 1-22 and 24-26 as lacking a sufficient written description are respectfully requested.

Claims 1-8, 10, 16-22 and 24-26 were rejected under 35 U.S.C. § 112, second paragraph, as being indefinite. Applicant respectfully disagrees with the rejections.

In reviewing a claim for compliance with 35 U.S.C. 112, second paragraph, the Examiner must consider the claim as a whole, in light of the specification and the knowledge of the prior art, to determine whether the claim apprises one of ordinary skill in the art of its scope and, therefore, serves the notice function required by 35 U.S.C. 112, second paragraph, by providing clear warning to others as to what constitutes infringement of the patent. See, *e.g.*, Solomon v. Kimberly-Clark Corp., 216 F.3d 1372, 1379, 55 USPQ2d 1279, 1283 (Fed. Cir. 2000). A claim is indefinite only if, when read in light of the specification, it is "insolubly ambiguous, and no narrowing construction can properly be adopted." Exxon Research & Eng'g Co. v. United States, 265 F.3d 1371, 1375, 60 USPQ2d 1272, 1276 (Fed. Cir. 2001); Allen Eng'g Corp. v. Bartell Indus., Inc., 299 F.3d 1336, 1349, 63 USPQ2d 1769, 1776 (Fed. Cir. 2002).

The Examiner maintains that claim 1 is indefinite for its recitation of "plant Vitamin C biosynthesis pathway." The enzymes deemed to be encompassed by the claims are described throughout Applicant's specification, such as, for example, at Figure 1. The source of the nucleic acids that encode these enzymes is not relevant, particularly since Applicant's claims do not have any limitations regarding the source of the nucleic acid. Rather, the claims are limited merely to the specific proteins recited having the described enzymatic activity. Thus, one of ordinary skill in the art would understand what is claimed, when the claims are read in light of the specification. See attached Declaration of Dr. Patricia Conklin.

The Examiner maintains that claims 2 and 10 are indefinite in their recitation of "said plant, or portion thereof, is a dicot." One of ordinary skill in the art would understand that the claims encompass plant cells obtained from dicots, protoplasts obtained from dicots, callus or tissue cultures obtained from dicots, and whole plants that are dicots. There is nothing indefinite regarding use of the term "portion thereof" in these claims. See attached Declaration of Dr. Patricia Conklin.

The Examiner maintains that the relative term "increasing" in claim 16 renders the claim indefinite. Applicant respectfully disagrees.

Definiteness problems often arise when words of degree are used in a claim. That some claim language may not be precise, however, does not automatically render a claim invalid. The question becomes whether one of ordinary skill in the art would understand what is claimed when the claim is read in light of the specification. See generally Anchor Wall Systems, Inc. v. Rockwood Retaining Walls, Inc., (Fed. Cir. No. 02-1592, 2003).

A person of ordinary skill in the art would understand the meaning of the term "increasing" and apply its plain, ordinary meaning. There is no requirement for Applicant to define this term, as it is a term that is known to virtually everyone and its meaning is quite clear. More particularly, one of ordinary skill in the art would understand that the claimed transgenic plants have increased Vitamin C relative to plants that are not so transformed. See attached Declaration of Dr. Patricia Conklin.

The Examiner maintains that claim 20 lacks antecedent basis for the limitation "said genetically engineered plant." Claim 20 is hereby amended to overcome the rejection.

In view of the foregoing amendments and remarks, Applicant respectfully submits that these amendments have fully addressed the Examiner's rejections, and that the claims are now in condition for allowance. Reconsideration and withdrawal of the rejection of claims 1-22 and 24-26 as being indefinite are respectfully requested.

**Conclusion**

Applicant believes the claims, as amended, are patentable over the prior art, and that this case is now in condition for allowance of all claims therein. Such action is thus respectfully requested. If the Examiner disagrees, or believes for any other reason that direct contact with Applicants' attorney would advance the prosecution of the case to finality, he is invited to telephone the undersigned at the number given below.

"Recognizing that Internet communications are not secured, I hereby authorize the PTO to communicate with me concerning any subject matter of this application by electronic mail. I understand that a copy of these communications will be made of record in the application file."

Respectfully Submitted:
**--Conklin et al.--**

By: Thomas T. Aquilla
**-- Thomas T. Aquilla, Reg. No. 43,473 --**
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Dated: September 17, 2003

PAGE: 1 VERIFICATION SUMMARY REPORT DATE: 09/09/2003

PATENT APPLICATION TIME: 13:31:59

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5, Norris, Susan R.
6, Last, Robert L.
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10,<130> BTI-41
12,<140> 09/441,318
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STATISTICS SUMMARY

Application Serial Number: 09/441,318
Alpha or Numeric: Numeric
Application Class:
Application File Date: 1999-11-16
Art Unit:
Software Application: PatentIN3.1
Total Number of Sequences: 6
Total Nucleotides: 615
Total Amino Acids: 0
Number of Errors: 0
Number of Warnings: 7

Number of Corrections: 0

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

September 17, 2003

| | |
|---|---|
| In re Application of: | Conklin *et al.* |
| Serial No. | 09/441,318 |
| Filed: | 11/16/99 |
| For: | TRANSGENIC PLANT WITH INCREASED EXPRESSION OF GDP-MANNOSE PYROPHOSPHORYLASE |
| Examiner: | Kubelik, A. |
| Art Unit: | 1638 |
| Confirmation No.: | 4166 |
| Attorney Docket No.: | BTI-41 |

HONORABLE COMMISSIONER OF
PATENTS AND TRADEMARKS
Washington, D.C. 20231

## DECLARATION UNDER 37 CFR § 1.132

In response to the Office Action dated June 17, 2003, I, Dr. Patricia L. Conklin, Ph.D., do hereby declare and say as follows:

## BACKGROUND INFORMATION

1. I am a former Research Scientist at the Boyce Thompson Institute for Plant Research. My ***curriculum vitae***, which describes my education, employment, research publications, patents and other expert qualifications, is attached hereto as Exhibit 1.

2. I have extensive experience in the fields of molecular biology and genetic engineering of plants. I have worked in the field of molecular biology since **19**__. Through my years of research and professional activities in the fields of molecular biology and genetic engineering, I am familiar with the skills of those working in the field from **19**__ to the present. In carrying out my current professional activities, I keep up to date on the technical literature and maintain contact with other experts in the field.

3. I am a co-inventor of the invention of claims 1-26 in the present patent application, Ser. No. 09/441,318.

4. I have read and understood the above referenced patent application, including the specification, claims and the relevant prior art. Based on my analysis of the contents of the

aforementioned documents. I have formulated certain opinions regarding the issues of the definiteness, written description and enablement of claims 1-22 and 23-26.

5. The standard I used for definiteness is whether the claim apprises one of ordinary skill in the art of its scope.

6. The standard I used for written description is whether the disclosure as originally filed reasonably conveys to one of ordinary skill in the art that the inventor had possession, at the time the application was filed, of the claimed subject matter.

7. The standard I used for enablement is whether one of ordinary skill in the art could make or use the claimed invention, at the time the application was filed, from the disclosure in the application coupled with information known in the art, without undue experimentation.

8. A person of ordinary skill in the art would have a Ph.D. in molecular biology or an equivalent degree and at least two years of laboratory research experience in plant biology, or at least a B.S. degree and a minimum of four years of laboratory research experience in plant biology.

9. Molecular biology, and particularly the genetic engineering of plants, are extremely complex subjects and therefore the art typically engages in complex, time-consuming experimentation.

10. The level of skill in the art is very high, as attested to by the level of ordinary skill noted above, and the state of the art is relatively advanced, in that complete manuals are available that describe the methods of molecular biology and transformation of plants in great detail.

**CLAIMS 1-8, 10, 16-22 and 24-26 ARE NOT INDEFINITE**

11. With regard to claim 1 and its dependent claims, the enzymes deemed to be encompassed by the claims are described at Figure 1. The source of the nucleic acids that encode these enzymes is not relevant, particularly since the claims do not have any limitations regarding the source of the nucleic acid. Rather, the claims are limited merely to the specific proteins recited having the described enzymatic activity. Thus, one of ordinary skill in the art would understand what is claimed, when the claims are read in light of the specification.

12. With regard to claims 2 and 10 and their dependent claims, one of ordinary skill in the art would understand that the claims encompass plant cells obtained from dicots, protoplasts obtained from dicots, callus or tissue cultures obtained from dicots, and whole plants that are dicots. There is nothing indefinite regarding use of the term "portion thereof" in these claims.

13. With regard to claim 16, a person of ordinary skill in the art would understand the meaning of the term "increasing" and apply its plain, ordinary meaning. There is no need to define this term, as it is a term that is known to virtually everyone and its meaning is quite clear. More particularly, one of ordinary skill in the art would understand that the claimed transgenic plants have increased Vitamin C relative to plants that are not so transformed.

**ENABLEMENT OF CLAIMS 1-22 and 24-26**

14. The specification provides ample guidance for the full-length gene encoding GMPase. Based on the disclosure of the GenBank Accession number, one of ordinary skill in the art would be able to obtain the full-length sequence of the GMPase gene without undue experimentation. Indeed, the cDNA encoding the *Arabidopsis* GDP-mannose pyrophosphorylase (EST ID #9908, GenBank #T46645, www.ncbi.nlm.nih.gov/irx/cgi-bin/birx_doc?dbest_cu+6850) can easily be obtained from the Arabidopsis Biological Resource DNA Stock Center (aims.cps.msu.edu/aims; Columbus, OH), as described in the specification. Thus, obtaining a clone of the full-length gene would not require any experimentation at all, let alone experimentation that is "undue."

17. The specification provides ample guidance for wild-type plants transformed with the GMPase gene, and for methods of making stress resistant plants by transformation with a nucleic acid encoding the GMPase gene. Indeed, the specification provides real examples of plants that were transformed with the full-length gene encoding GMPase (Specification at page 14 lines 1-6), and which exhibited increased Vitamin C levels (Specification at page 16 Table 1).

18. The prior art by Bauw et al. (WO 98/50558) teaches *Arabidopsis* and tobacco plants transformed with a gene encoding L-galactono-y-lactone dehydrogenase (pages 15-20), an enzyme involved in vitamin C biosynthesis. Increased vitamin C levels (Table 5) and increased stress resistance (page 2 lines 16-21) would be inherent properties of these plants. Thus, the prior art teaches that plants can be transformed with a gene encoding an enzyme in the Vitamin C pathway and thereby produce transgenic plants having increased Vitamin C and stress resistance.

19. Furthermore, by following the teachings in the specification, we subsequently identified another gene encoding another enzyme in the Vitamin C biosynthesis pathway, VTC4. See Ser. No. 09/909,600. The methods used to isolate this second gene were virtually identical to those in the present specification. Thus, clearly, the present specification provides enablement for the claimed invention.

20. Any alleged unpredictability associated with expression of genes in plants has been overcome, in that the gene encoding GMPase was, in fact, transformed into plants, thereby generating genetically engineered plants having increased levels of Vitamin C, relative to the progenitor plants.

21. Based on the fact that the prior art demonstrates that plants can be transformed with a gene encoding an enzyme in the Vitamin C pathway and thereby produce transgenic plants having increased Vitamin C and stress resistance, and further based on the extensive teachings in the present patent application, one of ordinary skill in the art would be able to practice the claimed invention without undue experimentation, and would reasonably expect that transformation of GMPase into a wild-type plant would increase the levels of Vitamin C and stress resistance in the resulting transgenic plants.

**WRITTEN DESCRIPTION OF CLAIMS 1-22 and 24-26**

22. Many of the genes encoding GMPase (including that of *Arabidopsis* and other species), as well as the other enzymes in the Vitamin C pathway, are known in the art.

23. Figure 1 and the specification at page 4, lines 12-16, disclose the enzymes in the Vitamin C pathway.

24. Furthermore, based on the examples and experimental results disclosed in the application, one of ordinary skill in the art would know that the Applicant was in possession of the GMP-mannose pyrophosphorylase gene and recombinant plants transformed with this gene that express increased levels of Vitamin C.

**CONCLUSION**

25. Based on the above analysis, I conclude that claims 1-22 and 24-26 in the present patent application are definite and supported by both a written description and an enabling disclosure.

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true, and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States

statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

Dated: Sept 17, 2003 By: _____
Dr. Patricia L. Conklin, Ph.D.

# EXHIBIT 1

## *Curriculum Vitae* of Dr. Patricia L. Conklin, Ph.D.

# CURRICULUM VITAE

**Patricia Lehman Conklin**

**Current Address:**

State University of New York College at Cortland
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**Education:**

Cornell University, Ithaca, NY., Doctoral Program, Section of Genetics and Development, Ph.D. May 1992.
University of North Carolina at Chapel Hill, Doctoral Program, Curriculum in Genetics, 1985-1986.
Allegheny College, Meadville, PA., Bachelor of Science; *summa cum laude*, Biology, 1985.

**Awards, Grants and Fellowships:**

SUNY Cortland "Excellence in Research and Scholarship" Award Recipient, 8 May 2003.
USDA-NRI Plant Responses to the Environment Program grant entitled "Molecular Mechanism of Plant Vitamin C Biosynthesis.", Nov. 02 – October 04, $117,374.
Subcontract Award under USDA-NRI Plant Responses to the Environment Program grant awarded to Dr. J. Sparks entitled "The controls over the assimilation and emission of atmospheric reactive nitrogen by leaves.", Cornell University, July 02 – June 04, $10, 415.
Travel Award from the Cortland College Foundation, May 03.
American Cancer Society Postdoctoral Fellow, Sept. 92 – Aug. 95.
Walter Schon Lenk Fellow, (Cornell University Graduate School Award) 1991-92 academic year.
Plant Science Center Fellow, Cornell University, June 89 – Sept 91 excluding spring 1990.
McKnight Training Grant, Cornell University, June 86 – Jan 89 excluding spring 1988.
Research Triangle Universities Plant Molecular Biology Fellow, University of North Carolina at Chapel Hill, 1985-86 academic year.
University of North Carolina at Chapel Hill Biotechnology Program Award, 1985.
Valedictorian-Allegheny College Class of 1985.
Phi Beta Kappa
Sandra Doane Turke Scholar, Allegheny College.
Robert E. Bugbee Award for Research in Biology, Allegheny College.
Biology Faculty Award for Scholarship in Biology, Allegheny College.

**Academic Experience:**

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| *Assistant Professor*<br>Department of Biological Sciences<br>State University of New York College at Cortland | 2001-present |
| *Visiting Assistant Professor*<br>Department of Biological Sciences<br>State University of New York College at Cortland | 2000-01 |
| *Adjunct Research Associate*<br>Boyce Thompson Institute for Plant Research at Cornell University | 2000-01 |
| *Sr. Research Associate*<br>Boyce Thompson Institute for Plant Research at Cornell University | 1999-00 |
| *Research Associate*<br>Boyce Thompson Institute for Plant Research at Cornell University | 1995-99 |
| *Postdoctoral Fellow with Dr. Robert L. Last*<br>Boyce Thompson Institute for Plant Research at Cornell University | 1992-95 |
| *Graduate Student with Dr. Maureen R. Hanson*<br>Cornell University, Section of Genetics and Development | 1986-92 |
| *Undergraduate Senior Comprehensive Project with Dr. Christine Nebiolo*<br>Allegheny College | 1984-85 |

**Teaching Experience:**

*Assistant Professor*, SUNY-Cortland, Bio312 (Genetics) Fall 2003, Spring 2003, Fall 2002, Spring 2002, Fall 2001; Bio 521 (Molecular Genetics) Fall 2003; Bio 306 (Human Genetics) Fall 2002, Spring 2002; Bio110 (Principle of Biology I) Fall 2001.

*Guest Lecturer* for Sci320 (Science, Technology and Culture - Dr. Brian Rivest). The impact of recombinant DNA technology on the field of human health. Spring 2003.

*Guest Lecturer* for Bio 310 (Dr. Steven Broyles) Plant Stress. How plants cope with drought and freezing temperatures. Summer 2002.

*Visiting Assistant Professor at SUNY-Cortland*, Bio 312 (Genetics), Bio 306 (Human Genetics) Fall semester 2000; Bio 312 (Genetics) Spring 2001.

*Guest Lecturer* for Sci300 (Dr. Kathy Russell) Genomics and Human Disease, Spring 2001, Fall 2001.

*Laboratory Leader for Cornell Institute for Biology Teachers* (CIBT), Ascorbic acid. Cornell University, 25 July 2000.

*Workshop Leader* at "Biology as an information science – a workshop for engineers." held for the Dept. of Engineering Faculty, Cornell University, 24 May 2000.

*Guest Lecturer*, Cornell PB606 (Advanced Plant Breeding). February 17, 2000, February 16, 1998.

*Instructor*, New Visions - Explorations in Biological Sciences Student Workshop at BTI, The genetics of vitamin C-deficient Arabidopsis mutants. 27 Feb.1998.

*Instructor*, Cornell Explorations Freshman Workshop, Vitamin C - good for you and good for plants. 5 December 1997.

*Instructor*, Return to Campus Workshop for high school biology students, Cornell Institute for Biology Teachers, Plant antioxidants. Fall 1997.

*Workshop Leader*, Stratospheric vs. Tropospheric Ozone: Why plants like one but not the other. Marple Newtown Freshman Initiative, Penn State University Great Valley Campus, Philadelphia, PA, sponsored by ARCO and the Marple Newtown School District. March 1997.

*Instructor*, Cornell University Adult University Course, The genie unleashed: DNA in the modern world. 7-13 July 1996.

*Instructor*, Cornell Explorations Freshman Workshop, Plants and the environment: Arabidopsis, ozone and vitamin C. 7 Nov 1995.

*Lecturer and Laboratory Instructor*, Cornell University Plant Science Center Workshop - Construction of cDNA libraries and RNA analysis. 2-13 August 1993.

*Teaching Assistant*, Cornell University; Introduction to genetics laboratory, Spring semester 1990; Plant molecular biology laboratory, Spring semester 1988.

*Workshop Leader* - Plant physiology and molecular biology, "Expanding Your Horizons" program for middle school girls. Fall 1989,1990,1993.

*Teaching Assistant*, Allegheny College, Cell biology laboratory, Spring 1984, 1985; Ecology laboratory, Fall 1983.

**Service Activities:**

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| Departmental Personnel Committee SUNY Cortland | 2003-04 |
| Honorary Degree Committee, SUNY Cortland | 2003-04 |
| Departmental Biology Awards Selection Committee member | 2002-03 |
| Senior Judge for Greater Syracuse Scholastic Science Fair | 2002-03 |
| Cortland Biology Newsletter Group | 2001-03 |
| President's Task Force Focus Group, SUNY Cortland | 2002 |
| Cortland Y.W.C.A Girl's Day Out Participant | 2001 |
| A & S College Curriculum Committee | 2001-03 |
| Department of Biological Sciences Curriculum Committee | 2001-03 |
| Biomedical Sciences Major Proposal Group, SUNY Cortland | 2002-03 |
| Biology Club Advisor, SUNY Cortland | 2000 |
| Boyce Thompson Library Committee | 1996-00 |
| Boyce Thompson Internal Seminar Series Committee | 1998-99 |
| Boyce Thompson Institute Management Advisory Committee | 1996-98 |
| Boyce Thompson Educational Outreach Committee | 1997-99 |
| Student Representative - Cornell University, Section of Genetics and Development Graduate Student Admissions Committee | 1990 |

**Professional Activities:**

*Ad hoc* reviewer for USDA-NRI Plant Responses to the Environment, National Science Foundation Integrative Plant Biology Program, National Science Foundation Integrative Plant Genome Research Program, *Plant Physiology*, *Plant Cell*, *The Plant Journal*, *Journal of Experimental Botany*, and *Plant Cell and Environment*

Member: American Association of Plant Physiology

USDA-NRI Plant Responses to the Environment Review Panel Member, Washington, D.C. 2-5 Feb. 2003.

Title III WebCT Workshop participant, SUNY Cortland, 19 May –20 May 2003.

Student Computer Access Program (SCAP) Award from the SCAP Committee for five G3 MacIntosh Computers and one inkjet printer for the molecular biology teaching laboratory, Fall 2002.

**Selected Public Presentations:**

*Poster Presentation*, **P. L. Conklin** and C. Barth "The ascorbate-deficient Arabidopsis mutant vtc1 has altered responses to both high light and pathogens." presented by P.L. Conklin at the Fourteenth International Conference on Arabidiopsis, Madison, WI. June 2003.

*Poster Presentation*, C. Barth, G.H. Krause, **P,L, Conklin** "What is wrong with *soz2*? A genetic and physiological characterization of the ozone-sensitive *Arabidopsis thaliana* mutant *soz2*" presented by C. Barth at the Thirteenth International Conference on Arabidopsis, Seville, Spain. July 2002.

*Poster Presentation*, C. Barth and **P.L. Conklin**. Annual Meeting of the American Society of Plant Biologists, Providence, RI. July 2001

*Poster Presentation*, J.A. Brenchley, G.L. Wheeler, S. Gatzek, N. Smirnoff, **P.L. Conklin**. Annual Meeting of the American Society of Plant Biologists, Providence, RI. July 2001.

*Invited Speaker*, The Ascorbate Biosynthetic Pathway. XVI International Botanical Congress, St. Louis, MO. August 1999.

*Invited Speaker*, Oxidative Stress Adaptation: Mutants and Mechanisms in Arabidopsis. Plant Molecular Biology Gordon Conference, Plant Biological Regulator Mechanisms, Henniker, NH. July 1998.

*Poster Presentation*, S.A. Saracco, **P.L. Conklin**, S.R. Norris, G.L. Wheeler, N. Smirnoff, R.L. Last. The Biochemical Genetics of Ascorbate Biosynthesis in Arabidopsis. Ninth International Conference on Arabidopsis Research, Madison, WI. June 1998.

*Speaker*, Ascorbic Acid Biosynthesis in Plants: A Molecular Genetic Approach. Cereon Genomics Discovery Group, Cambridge, MA. June 1998.

*Invited Speaker*, Ozone-sensitive Arabidopsis Mutants. Eighth International Conference on Arabidopsis Research, Madison, WI. June 1997.

*Invited Speaker*, Antioxidant status in Ozone-Sensitive Arabidopsis Mutants. The Plant Workshop: Leaves, La Colle sur Loup, France. June 1997.

*Invited Speaker*, Ascorbate-Deficient Arabidopsis Mutants. VIII Biennial Meeting International Society for Free Radical Research, Barcelona, Spain. October 1996.

*Invited Speaker*, Cornell University Plant Biology Seminar Series, Ithaca, NY. June 1996.

*Selected Oral Presentation*, 1995 Annual Meeting of the American Society of Plant Physiologists, Charlotte, NC. 8/95.

*In-House Section of Genetics and Development Seminar Series*, Cornell University, Ithaca, NY. 9/88, 3/90, 3/91, 5/92, 3/94, 3/95, 3/96, 3/97.

*Invited Speaker*, 26th Air Pollution Workshop, Boyce Thompson Institute at Cornell University, Ithaca, NY. 3/94.

*In-House Boyce Thompson Institute Seminar Series*, Boyce Thompson Institute at Cornell University, Ithaca, NY. 4/93, 3/96, 3/97, 3/98, 3/99.

*Seminar Speaker*, Dept. of Biology, Allegheny College, Meadville, PA. 10/91.

*Invited Plenary Speaker*, IVth International Workshop on Plant Mitochondria, Cornell University, Ithaca, NY. 9/90.

**Published Abstracts:**

Kliebenstein, D.J., **P.L. Conklin**, L.G. Landry, E.H. Williams, and R.L. Last (1997) Arabidopsis mutants altered in antioxidant enzyme accumulation. *Plant Physiol* 114(3S):56. 1997 Annual Meeting of the American Society of Plant Physiologists, Vancouver, B.C.

Last, R.L., L.G. Landry, B.-C. Kim, and **P.L. Conklin** (1997) UV-B protective mechanisms in plants: sensing avoidance, and repair. *Photochem Photobiol*, 65:77S.

**Conklin, P.L.** and R.L. Last (1995) Isolation of ozone hypersensitive mutants in *Arabidopsis thaliana*. *Plant Physiol* 108(2S):35. 1995 Annual Meeting of the American Society of Plant Physiologists, Charlotte, NC.

Connett, M.B., **P.L. Lehman** and M.R. Hanson (1989) Plant transformation as a test of the relationship between cytoplasmic male sterility, respiratory phenotype, and the *pcf* gene. *J. Cell* Biochem, 13D: 299. UCLA Symposium on Molecular and Cellular Biology - Plant Gene Transfer, Park City, UT.

**Lehman, P.L.** and M.R. Hanson (1988) Analysis of *atp9* genes in *Petunia hybrida*. *Genome*, 30 (Suppl. 1). XVIth Intl. Congress of Genetics, Toronto.

**Publications:**

KochHar, S., C.B. Watkins, **P.L. Conklin**, and S.K. Brown (2003) A quantitative and qualitative analysis of antioxidant enzymes in relation to susceptibility of apples to superficial scald. *J. Amer. Soc. Hort. Sci. in press.*

Barth, Carina and **P.L. Conklin** (2003) The lower cell density of leaf parenchyma in the *Arabidopsis thaliana* mutant *lcd1-1* is associated with increased sensitivity to ozone and virulent *Pseudomonas syringae*. *The Plant J.*, 35: 206-218.

Müller-Moulé, P., **P. Conklin**, and K.K. Niyogi (2002) Ascorbate-deficiency limits violazanthin de-epoxidase activity *in vivo*. *Plant Physiol*, 128:970-977.

Smirnoff, N., **P.L. Conklin**, and F.A Loewus. (2001) Biosynthesis of ascorbic acid in plants - a renaissance. *Ann Review Plant Physiol and Plant Mol Bio*, 52: 437-467.

**Conklin, P.L.** (2001) Recent advances in the role and biosynthesis of ascorbic acid in plants. *Plant Cell Environ*, 24: 383-394.

Lukowitz, W., T.C. Nickle, D.W. Meinke, R.L. Last, **P.L. Conklin**, and C. Somerville (2001) Arabidopsis *cyt1* mutants are deficient in a mannose-1-phosphate guanosyltransferase and point to a requirement of N-linked glycosylation for cellulose biosynthesis. *Proc Natl Acad Sci USA*, 98:2262-2267.

**Conklin, P.L.**, S.A. Saracco, S.R. Norris, and R.L. Last (2000) Identification of vitamin C-deficient *Arabidopsis thaliana* mutants. *Genetics*, 154: 847-856.

**Conklin, P.L.,** S.R. Norris, G.L. Wheeler, E.H. Williams, N. Smirnoff, and R.L. Last (1999) Genetic evidence for the role of GDP-mannose in plant ascorbic acid (vitamin C) biosynthesis. *Proc Natl Acad Sci USA*, 96: 4198-4203.

**Conklin, P.L.** (1998) Vitamin C: a new pathway for an old antioxidant. Trends Plant Sci., 3:329-330.

**Conklin, P.L.**, J.E. Pallanca, R.L. Last and N. Smirnoff. (1997) L-ascorbic acid metabolism in the ascorbate deficient Arabidopsis mutant *vtc1*. *Plant Physiol*, 115: 1277-1285.

**Conklin, P.L.**, E.W. Williams and R.L. Last. (1996) Environmental stress sensitivity of an ascorbic acid-deficient Arabidopsis mutant. *Proc Nat Acad Sci USA*, 93:9970-9974.

**Conklin, P.L.** and R. L. Last (1995) Differential accumulation of antioxidant enzyme mRNAs in *Arabidopsis thaliana* exposed to ozone. *Plant Physiol*, 109: 203-212.

Ormrod, D.P., L.G. Landry and **P.L. Conklin** (1995) Short-term UV-B radiation and ozone exposure effects on aromatic secondary metabolite accumulation and shoot growth of flavonoid-deficient Arabidopsis mutants. *Physiol Planta*, 93: 602-610.

**Conklin, P.L.** and M.R. Hanson (1994) Recombination of plant mitochondrial genomes. In "Homologous recombination and Gene Silencing in plants." Ed. J. Paszkowski. Kluwer Academic Publishers, The Netherlands, pp. 61-81.

**Conklin, P.L.** and M.R. Hanson (1993) A truncated recombination repeat in the mitochondrial genome of a Petunia CMS line. *Curr Genet*, 23: 477-482.

Hanson, M.R., C.A. Sutton, B. Lu, **P.L. Conklin**, H. Wintz, R. Wilson and K.D. Pruitt. 1993. RNA editing in Petunia mitochondria. *In:* Plant Mitochondria. A. Brennicke and U. Kuck, eds. VCH Publishers, NY, pp. 71-81.

Sutton, C.A., **P.L. Conklin**, K.D. Pruitt, A.J. Calfee, A.G. Cobb and M.R. Hanson (1993) Editing of *rps3/rpl16* transcripts creates a premature truncation of the *rpl16* reading frame. *Curr.Genet*, 23: 472-476.

**Conklin, P.L.**, R.K. Wilson and M.R. Hanson (1991) Multiple *trans*-splicing events are required to produce a mature *nad1* transcript in a plant mitochondrion. *Genes and Dev*, 5: 1407-1415.

**Conklin, P.L.** and M.R. Hanson (1991) Ribosomal protein S19 is encoded by the mitochondrial genome in *Petunia hybrida*. *Nucl Acids Res*, 19: 2701-2705.

Sutton. C.A., **P.L. Conklin**, K.D. Pruitt, and M.R. Hanson (1991) Editing of pre-mRNAs can occur before *cis*- and *trans*-splicing in *Petunia* mitochondria. *MolCell Biol*, 11: 4274-4277.

Rockwell, B.H., **P.L. Lehman** and C.M. Nebiolo (1985) Long term heat shock in maize seedlings. *Maize Genetics Coop Newsletter*, 59: 78.